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Serial No. 09/831,754

Amendments to the Specification:

Rewrite page 2, line 20 – page 9, line 25, as:

The invention features an isolated nucleic acid molecule encoding a protein molecule whose amino acid sequence comprises the sequence shown in SEQ ID NO: 1 as well as the protein molecule according to SEQ ID NO: 1. Hereinafter, the protein molecule of SEQ ID NO: 1 is denoted "SELADIN-1". One function of SELADIN-1 is to protect cells against degeneration and cell death. In particular, cells of the nerve system, muscular system, prostate, stomach, testis, ovary, adrenal glands, mammary glands, liver, spleen, lung, trachea or placenta are protected against degeneration and/or cell death. Therefore, the present invention also features functional variants of SELADIN-1 which might have a modification of the given primary structure of SELADIN-1, but whose essential biological function remains unaffected. "Variants" of a protein molecule shown in SEQ ID NO: 1 include for example proteins with conservative amino acid substitutions in highly conservative regions. For example, isoleucine, valine and leucine can each be substituted for one another. Aspartate and glutamate can be substituted for each other. Glutamine and asparagine can be substituted for each other. Serine and threonine can be substituted for each other. Amino acid substitutions in less conservative regions include e. g.: Isoleucine, valine and leucine can each be substituted for one another. Aspartate and glutamate can be substituted for each other. Glutamine and asparagine can be substituted for each other. Serine and threonine can be substituted for each other. Glycine and alanine can be substituted for each other. Alanine and valine can be substituted for each other. Methionine can be substituted for each of leucine, isoleucine or valine, and vice versa. Lysine and arginine can be substituted for each other. One of aspartate and glutamate can be substituted for one of arginine or lysine, and vice versa. Histidine can be substituted for arginine or lysine, and vice versa. Glutamine and glutamate can be substituted for each other. Asparagine and aspartate can be substituted for each other. Other examples of protein modifications include glycosilation and further post translational modifications. The invention also features the nucleic acid molecules encoding such functional variants of the protein molecule of SEQ ID NO: 1. Nucleic

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acid molecules can be DNA molecules, such as genomic DNA molecules or cDNA molecules, or RNA molecules, such as mRNA molecules. In particular, said nucleic acid molecule can be a cDNA molecule comprising a nucleotide sequence of SEQ ID NO: 2. The invention also features an isolated DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions. Examples for stringent conditions include (i) 0.2xSSC (standard saline citrate) and 0.1 % SDS at 60 C and (ii) 50 % formamide, 4xSSC, 50 mM HEPES, pH Denhardt's solution, 100 µg/ml thermally denatured salmon sperm DNA at 42 °C.

In another aspect, the invention features a vector comprising a nucleic acid encoding a protein molecule shown in SEQ ID NO: 1. It also features a vector comprising a nucleic acid molecule encoding a protein molecule, the function of which is to protect cells against degeneration and/or cell death, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof. In preferred embodiments, a virus, a bacteriophage, or a plasmid comprises the described nucleic acid. In particular, a plasmid adapted for expression in a bacterial cell comprises said nucleic acid molecule, e. g. a nucleic acid molecule encoding a protein molecule shown in SEQ ID NO: 1, and the regulatory elements necessary for expression of said molecule in the bacterial cell. In a further aspect, the invention features a plasmid adapted for expression in a yeast cell which comprises said nucleic acid molecule, e. g. a nucleic acid molecule encoding a protein molecule shown in SEQ ID NO: 1, and the regulatory elements necessary for expression of said molecule in the yeast cell. In another aspect, the invention features a plasmid adapted for expression in a mammalian cell which comprises a nucleic acid molecule, e. g. a nucleic acid molecule encoding a protein molecule shown in SEQ ID NO: 1, and the regulatory elements necessary for expression of said molecule in the mammalian cell.

In a further aspect, the invention features a cell comprising a nucleic acid molecule encoding a protein molecule shown in SEQ ID NO: 1. The invention also features cells comprising a nucleic acid molecule encoding a protein molecule whose function is to protect cells against

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degeneration and/or cell death and whose amino acid sequence comprises the sequence shown in SEQ ID NO: ~~NO:~~ 1 or a functional variant thereof. It also features cells comprising a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions. In preferred embodiments, said cell is a bacterial cell, a yeast cell, a mammalian cell, or a cell of an insect. In particular, the invention features a bacterial cell comprising a plasmid adapted for expression in a bacterial cell, said plasmid comprising a nucleic acid molecule which encodes a protein molecule shown in SEQ ID NO: ~~NO:~~ 1, and the regulatory elements necessary for expression of said molecule in the bacterial cell. The invention also features a yeast cell comprising a plasmid adapted for expression in a yeast cell, said plasmid comprises a nucleic acid molecule encoding a protein molecule shown in SEQ ID NO: ~~NO:~~ 1, and the regulatory elements necessary for expression of said molecule in the yeast cell. It further features a mammalian cell comprising a plasmid adapted for expression in a mammalian cell, said plasmid comprising a nucleic acid molecule which encodes a protein molecule shown in SEQ ID NO: ~~NO:~~ 1, and the regulatory elements necessary for expression of said molecule in the mammalian cell.

The invention further features an antibody specifically immunoreactive with an immunogen, wherein said immunogen is shown in SEQ ID NO: ~~NO:~~ 1 or wherein said immunogen is a protein molecule, the function of which is to protect cells against degeneration and/or cell death, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO:~~ 1 or a functional variant thereof. In another aspect, the invention aims at a method of detecting pathological cells in a subject which comprises immunocytochemically staining cells with the aforementioned antibody, wherein a low degree of staining in said cell compared to a reference cell representing a known health status indicates a pathological change of said cell. The invention is particularly suited to detect pathological structures in the brain of a subject-the detection method comprises immunocytochemically staining said pathological structures with said antibody. It is also especially suited to detect pathological cells of the muscular system, prostate, stomach, testis, ovary, adrenal glands, mammary glands, liver, spleen, lung, trachea or placenta.

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In another aspect, the invention features a method of diagnosing or prognosing a disease, in particular a neurological disease, in a subject comprising: determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (c) a protein molecule wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f),

and comparing said level, or said activity, or both said level and said activity, of at least one of said substances (a) to (h) to a reference value representing a known disease or health status, thereby diagnosing or prognosing a disease, in particular a neurological disease, in said subject.

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In another aspect, the invention features a method of monitoring the progression of a disease, in particular a neurological disease, in a subject, comprising:

determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f),

and comparing said level, or said activity, or both said level and said activity, of at least one of said substances (a) to (h) to a reference value representing a known disease or health status, thereby monitoring progression of a disease, in particular a neurological disease, in said subject.

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In still a further aspect, the invention features a method of evaluating a treatment for a disease, in particular a neurological disease, in a subject, said method comprising:

determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f),

and comparing said level, or said activity, or both said level and said activity, of at least one of said substances (a) to (h) to a reference value representing a known disease or health status, thereby evaluating a treatment for a disease, in particular a neurological disease, in said subject.

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In a further aspect, the invention features a kit for diagnosis, or prognosis of a disease, said kit comprising:

- (1) at least one reagent which is selected from the group consisting of reagents that selectively detect
 - (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
 - (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
 - (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
 - (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
 - (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
 - (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
 - (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
 - (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f),
- (2) instructions for diagnosing, or prognosing said disease by
 - (i) detecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (h) in a sample from said subject;

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and

- (ii) diagnosing, or prognosing said disease, wherein
a varied level, or activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (h) compared to a reference value representing a known health status;
or a level, or activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (h) similar or equal to a reference value representing a known disease status indicates diagnosis, or prognosis of said disease.

Rewrite page 10, 2nd full ¶, as:

In another preferred embodiment, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO~~: 2 encodes a protein molecule, the function of which is to protect cells against cell degeneration and/or cell death.

Rewrite page 10, last ¶, as:

According to the present invention, a reduction in the level, or activity, or both said level and said activity, of (i) a transcription product of a DNA molecule encoding a protein molecule, whose amino acid sequence comprises the sequence shown in SEQ ID NO: ~~NO~~: 1 or a functional variant thereof or (ii) a protein molecule whose amino acid sequence comprises the sequence shown in SEQ ID NO: ~~NO~~: 1 or a functional variant thereof, in a sample from said subject relative to a reference value representing a known health status indicates the presence of a pathological status in said subject. In particular, a reduction in the level, or activity, or both said level and said activity of SELADIN-1 or *SELADIN-1* transcripts in said subject's brain regions affected heavily by neurodegeneration relative to a reference value representing a known health status indicates a diagnosis or prognosis of

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Alzheimer's disease. Predominantly neurons within the inferior temporal lobe, the entorhinal cortex, the hippocampus and the amygdala degenerate in Alzheimer's disease.

Rewrite the ¶ bridging pages 11 and 12 as:

In preferred embodiments, said level or activity of the protein molecule shown in SEQ ID NO: ~~NO:~~ 1, or a functional variant or fragment thereof, is detected using an immunoassay. These assays can measure the amount of binding between said protein molecule and an anti-protein antibody, e.g. an anti-SELADIN-1 antibody, by the use of enzymatic, chromodynamic, radioactive, or luminescent labels which are attached to either the antiprotein antibody or a secondary antibody which binds the anti-protein antibody. In addition, other high affinity ligands may be used. Immunoassays which can be used include e. g. ELISAs, Western blots and other techniques known to those of ordinary skill in the art (see Harlow et al., Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

Rewrite page 12, 2nd full ¶, as:

Monoclonal antibodies capable of recognizing a protein molecule of SEQ ID NO: ~~NO:~~ 1 or a functional variant or fragment thereof can be prepared using methods known in the art (see e. g. Köhler and Milstein, Nature 256,495-497 1975; Kozbor et al., Immunol. Today 4,72,1983; Cole et al., Monoclonal antibodies and cancer therapy, Alan R. Liss, Inc., pp 77-96,1985; Marks et al., J. Biol. Chem., 16007-16010,1992; the contents of which are incorporated herein by reference). Such monoclonal antibodies or fragments thereof can also be produced by alternative methods known to those of skill in the art of recombinant DNA technology (see e.g. Sastry et al, PNAS 86: 5728,1989;; Watson et al., Rekombinierte DNA, 2nd ed., Spektrum Akademischer Verlag GmbH, 1993; Watson et al, Recombinant DNA, 2nd ed., W. H. Freeman and Company, 1992; the contents of which are incorporated herein by reference). Monoclonal antibodies useful in the methods of the invention are

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directed to an epitope of SELADIN-1 or a functional variant or fragment thereof, such that the complex formed between the antibody and SELADIN1, or between the antibody and said functional variant or fragment, can be recognized in detection assays. The term "antibodies" encompasses all forms of antibodies known in the art, such as polyclonal, monoclonal, chimeric, recombinatorial, single chain antibodies as well as fragments thereof which specifically bind to *SELADIN-1*, or to a functional variant or fragment thereof.

Rewrite the ¶ bridging pages 13 and 14 as:

In another aspect, the invention features a method of treating or preventing a disease, in particular a neurological disease, in a subject comprising administering to said subject in a therapeutically effective amount an agent or agents which affect a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: NO: 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: NO: 2 under stringent conditions,

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- (f) a translation product of a DNA-molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f).

Rewrite page 14, 2nd full ¶, as:

In another preferred embodiment, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 encodes a protein molecule, the function of which is to protect cells against cell degeneration and/or cell death.

Rewrite page 23, ¶¶ 3 and 4, as:

Figure 13 discloses the protein sequence of *SELADIN-1* (SEQ ID NO: 1). The full length protein consists of 516 amino acid residues. The sequence is given in the one letter amino acid code.

~~Figure 14~~ Figures 14A-14C discloses the nucleotide sequence of the cloned *SELADIN-1* cDNA (SEQ ID NO: 2) comprising 4248 nucleotides. The coding sequence for the *SELADIN-1* protein starts at nucleotide position 100 and stops at position 1648.

Rewrite page 16, line 3 - page 20, line 25, as:

In another aspect, the invention features an agent which affects an activity, or level, or both said activity or level, of at least one substance which is selected from the group consisting of

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- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID ~~NO:~~ NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID ~~NO:~~ NO: 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID ~~NO:~~ NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID ~~NO:~~ NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID ~~NO:~~ NO: 2 under stringent conditions,
- (f) a translation product of a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID ~~NO:~~ NO: 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f).

Preferably, the function of said protein molecule or a variant thereof is to protect cells from degeneration and/or cell death. Preferably, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID ~~NO:~~ NO: 2 encodes a protein, whose function is to protect cells from degeneration and/or cell death.

In another aspect, the invention features a medicament comprising such an agent.

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In still another aspect, the invention features an agent for treating or preventing a disease, in particular a neurological disease, which agent affects an activity, or level, or both said activity or level, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO:~~ 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO:~~ 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO:~~ 1 or a functional variant thereof
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
- (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
- (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f).

In preferred embodiments, said diseases are degenerative states characterized by cell degeneration or cell death or Alzheimer's disease and related neurofibrillary disorders.

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Further examples of neurological diseases are Parkinson's disease, Huntington disease, Amyotrophic lateral sclerosis, Pick's disease.

Preferably, the function of said protein molecule or a variant thereof is to protect cells from degeneration and/or cell death. Preferably, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 encodes a protein, whose function is to protect cells from degeneration and/or cell death.

In a further aspect, the invention features the use of an agent, for preparation of a medicament for treating or preventing a neurological disease, which agent affects an activity, or level, or both said activity or level, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: 1 or a functional variant thereof,
- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,
- (g) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: 2 under stringent conditions,

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- (h) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
- (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f).

Preferably, the function of said protein molecule or a variant thereof is to protect cells from degeneration and/or cell death. Preferably, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO~~ 2 encodes a protein molecule, whose function is to protect cells against degeneration and/or cell death.

In preferred embodiments, said diseases are Alzheimer's disease and related neurofibrillary disorders, or degenerative states, in particular neurodegenerative states, characterized by cell degeneration or cell death. Further examples of neurological diseases are Parkinson's disease, Huntington disease, Amyotrophic lateral sclerosis, Pick's disease.

In a further aspect, the invention features a method for identifying an agent that affects an activity, or level, or both said activity or level, of at least one substance which is selected from the group consisting of

- (a) a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO~~ 1 or a functional variant thereof,
- (b) a transcription product of a DNA molecule encoding a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO~~ 1 or a functional variant thereof,
- (c) a protein molecule, wherein the amino acid sequence of the protein molecule comprises the sequence shown in SEQ ID NO: ~~NO~~ 1 or a functional variant thereof,

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- (d) a DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
 - (e) a transcription product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
 - (f) a translation product of a DNA molecule, wherein said DNA molecule is capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 under stringent conditions,
 - (g) a molecule affecting a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of (a) to (f),
 - (h) a molecule which is affected in its level, or its activity, or both its level and activity, by at least one substance which is selected from the group consisting of (a) to (f),
- comprising the steps of:
- (i) providing a sample containing at least one substance which is selected from the group consisting of (a) to (f),
 - (ii) contacting said sample with at least one agent,
 - (iii) comparing an activity, or level, or both said activity and level, of at least one of said substances before and after contacting.

Preferably, the function of said protein molecule or a variant thereof is to protect cells from degeneration and/or cell death. Preferably, said DNA molecule capable of hybridizing with the complement of the cDNA described in SEQ ID NO: ~~NO:~~ 2 encodes a protein molecule, whose function is to protect cells against degeneration and/or cell death.

Rewrite the paragraph comprising page 26 as:

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Figure 18 shows the expression of *Seladin-1* in rat brain. *In situ* hybridization on paraformaldehyde fixed cryostat sections was performed as described by Hartman et al. (Developmental Neuroscience 17,246,1995). A 650 bp and a 900 bp fragment of the open reading frame of *Seladin-1* were PCR amplified using the following primer pairs:

1s (76-99) 5'GCG CTT ACC GCG CGG CGC CGC ACC 3' (SEQ ID NO: NO:3)

1as (749-726) 5'GAC CAG GGT ACG GCA TAG AAC AGG 3' (SEQ ID NO: NO: 4)

3s (803-826) 5'AGA AGT ACG TCA AGC TGC GTT TCG 3' (SEQ ID NO: NO: 5) and

3as (1749-1726) 5'TTC TCT TTG AAA GTG TGG ATC TAG 3' (SEQ ID NO: NO: 6).

PCR fragments were cloned in pGEM-Teasy vector (Promega), cut with EcoRI and cloned in pBluescript KS+. The orientation of the EcoRI cloned fragments was analyzed by PCR. Using the Ambion Maxiscript kit, ³⁵S-UTP labeled antisense and sense riboprobes were generated on NotI and ClaI linearized plasmids with T3 and T7-Polymerase, respectively, according to the manufacturers instructions. Hybridized sections were dipped in NTB-3 photographic emulsion (Kodak), exposed for 5 weeks and counterstained in Mayer's hemalum. A, D, G show photomicrographs of the emulsion dipped sections. **pvn** paraventricular nucleus, **bnM** basal nucleus of Meynert, **amy** amygdala, **ocmn** oculomotor nucleus, **rn** red nucleus, **fn** facial nucleus. B is a darkfield illumination blow up of the hippocampal region. **dg** dentate gyrus. C is a darkfield illumination blow up of the cortical layer five **cl V**. E, H show brightfield higher magnification photomicrographs of the regions of interest from D and G. F, I DIC (differential interference contrast) illuminations in higher magnification of E and H to demonstrate single neurons stained with silver grains. In rat brain, expression of *SELADIN-1* was high in the hippocampal region CA3 (Fig. 18 A, B), in the pyramidal neurons of cortical layer five (Fig. 18 A, C), in the amygdala (Fig. 18 A), in the magnocellular neurons of the basal nucleus of Meynert (Fig. 18 A) and in the reticular zone of the substantia nigra (data not shown). In addition, transcripts were also detected in several brain nuclei including the paraventricular nucleus (Fig. 18 A), the oculomotor nucleus (Fig. 18 D, E), the facial nucleus (Fig. 18 G, F) as well as the red nucleus (Fig. 18 D, E).

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Rewrite the 2nd full paragraph at page 31 as:

Total RNA from post-mortem brain tissues was prepared by using the RNeasy kit (Qiagen). The RNA preparations were treated with DNase I (Boehringer Mannheim) together with RNasin (Promega) for 30 minutes, followed by phenol extraction, and ethanol precipitation. 0.2 mg of each RNA preparation were transcribed to cDNA by using Expand Reverse Transcriptase (Boehringer Mannheim) with one base anchor primers HT11 A, HT1 the following PCR reaction, the cDNAs were amplified by using HT11 A along with the random primers HAP-5 (5'-TGCCGAAGCTTGGAGCTT-3') (SEQ ID NO: 9) and HAP3-T (5'-TGCCGAAGCTTGGTCAT-3') (SEQ ID NO: 10). Taq polymerase (AmpliTaq, Perkin Elmer Corp.), dGTP, dCTP, and dTTP (Amersham Pharmacia Biotech) and (α^{35} S)-dATP (NEN life science products) were used in a PCR protocol according to Zhao et al. The PCR products were separated on 6% polyacrylamide-urea sequencing gels that were dried subsequently on 3 mm filter paper (Whatman), and X-ray films (Dupont) were exposed for 12 hours.